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APPLICATION NO.	DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.	
10/696,752	10/29/2003	Sylvain Gilat	0126-UTL	7561	
32004 GALILEO PH	7590 01/23/2008 ARMACEUTICALS, INC.		EXAM	INER	
5301 PATRICI	K HENRY DRIVE		OLSEN, KAJ K		
SANTA CLAF	(A, CA 95054		ART UNIT	PAPER NUMBER	
			1795		
	•				
		•	MAIL DATE	DELIVERY MODE	
•	•		01/23/2008	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

		Application No.	Applicant(s)
		10/696,752	GILAT ET AL.
	Office Action Summary	Examiner	Art Unit
		Kaj K. Olsen	1795
Period fo	- The MAILING DATE of this communication app or Reply	ears on the cover sheet with the c	orrespondence address
	ORTENED STATUTORY PERIOD FOR REPLY	IS SET TO EXPIRE 3 MONTH	S) OR THIRTY (30) DAYS,
WHIC - Exter after - If NO - Failu	HEVER IS LONGER, FROM THE MAILING DATE of time may be available under the provisions of 37 CFR 1.13 SIX (8) MONTHS from the mailing date of this communication. It period for reply is specified above, the maximum statutory period were to reply within the set or extended period for reply with, by statute, reply received by the Office later than three months after the mailing and patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION  86(8). It no event, however, may a reply be the  will apply and will expire SIX (8) MONTHS from  cause the application to become ABANDONE	V. nety filed the mailing date of this communication. D (35 U.S.C. § 133).
Status			·
1)⊠	Responsive to communication(s) filed on 26 Se	eptember 2007.	
2a)□		action is non-final.	
3)	Since this application is in condition for allowar	nce except for formal matters, pro	osecution as to the merits is
	closed in accordance with the practice under E	Ex parte Quayle, 1935 C.D. 11, 45	53 O.G. 213.
Disposit	ion of Claims		
4)⊠	Claim(s) 1-58 is/are pending in the application.		
•	4a) Of the above claim(s) 9,20-25,32,37-49,54,	55 and 58 is/are withdrawn from	consideration.
•	Claim(s) is/are allowed.		
6)⊠	Claim(s) 1-4,7 and 8 is/are rejected.		
7)⊠	Claim(s) <u>5,6,10-19,26-31,33-36,50-53,56 and</u>	5/ is/are objected to.	
8)□	Claim(s) are subject to restriction and/o	r election requirement.	
Applicat	ion Papers		
9)□	The specification is objected to by the Examine	er.	
10)	The drawing(s) filed on is/are: a) acc	epted or b) objected to by the	Examiner.
	Applicant may not request that any objection to the	drawing(s) be held in abeyance. Se	e 37 CFK 1.85(a).
	Replacement drawing sheet(s) including the correct	tion is required if the drawing(s) is of	Action or form PTO-152
11)	The oath or declaration is objected to by the Ex	caminer. Note the attached Office	ACTION OF IGHT F 10-132.
	under 35 U.S.C. § 119		
	Acknowledgment is made of a claim for foreign	priority under 35 U.S.C. § 119(a	)-(d) or (f).
a)	☐ All b)☐ Some * c)☐ None of:		
	1. Certified copies of the priority document	is have been received.	ion No
	2. Certified copies of the priority document	is have been received in Applicat	ad in this National Stage
	3. Copies of the certified copies of the prior	(DCT Pule 17 2/a))	
l .	application from the International Burea See the attached detailed Office action for a list	of the certified copies not receive	ed.
•	See the attached detailed Office action for a list	of the certified adhies her reserve	<del></del> -
Attachme	* *	4) Interview Summan	y (PTO-413)
2) Noti	ice of References Cited (PTO-892). ice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail C 5) Notice of Informal	)ate
3) XI tofo	rmation Disclosure Statement(s) (PTO/SB/08) er No(s)/Mail Date <u>10-29-03:12-30-03:6-14-04</u> .	5) Notice of Information 6) Other:	Latest Ahirenni

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## **DETAILED ACTION**

## Election/Restrictions

1. Applicant's election without traverse of group I in the reply filed on 9-26-2007 is acknowledged. Applicant's election of species A and sub-species Ab is also acknowledged. Claims 9, 20-25, 32, 37-49, 54, 55, and 58 are withdrawn from consideration as being drawn to non-elected inventions.

# Claim Rejections - 35 USC § 103

- 2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
  - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
- 3. Claims 1, 3, 4, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al (Analytical Sciences, 17, May 2001, pp. 599-604) in view of Saskia et al (Free Radical Biology & Medicine, 30(3), 1996, pp. 331-342).
- 4. Yang discloses a method of identifying and selecting therapeutic compounds having a predetermined core structure (flavonoids) comprising establishing a relationship between a physical-chemical profile (oxidation potential) and a biological activity where the biological activity is measured in an assay (50% inhibition of lipid peroxidation (IC<sub>50</sub>)) effective in detecting compounds (flavanoids), which Saskia evidences can be utilized for targeted disorders. See Yang, "Results" on pp. 600-602, and see Saskia, discussion on p. 335. Yang does not

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explicitly disclose testing further potential therapeutic candidates with said core structure for the physical-chemical properties and selecting them based on a range predefined by the physicalchemical/biological relationship. However, Yang states that "this method [relating the half-wave potential to IC<sub>50</sub>] is expected to be useful for the quick screening of flavonoid antioxidants" (see abstract) and "the method established herein is expected to be a simple method for screening flavanoid antioxidants and estimating the AA [antioxidant activity] of flavonoid-containing foods and medicinal plants" (see the conclusion). Hence the purpose disclosed by Yang for relating the physical-chemical property to a biological activity for the select flavonoids screened is for the purpose of providing a future screening of other flavonoid containing substances. It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the established relationship defined by Yang for the study of further flavonoids so as to provide a quick screening of additional compounds without having to resort to a time consuming and labor intensive LPO assay for every particular compound of interest. Yang also does not explicitly disclose utilizing a predefined range from the physical-chemical/biological relationship. However, Yang relates the physical-chemical property (oxidation potential) to concentration of flavonoid needed for 50% inhibition (see fig. 4 and equation 3 on p. 602) (i.e. Yang is relating the oxidation potential to a particular efficacy of the flavonoid). Saskia teaches in a similar assay relating electrochemical response of flavonoids to its biological efficacy that the range of responses can be classified as indicating good, moderate, or bad inhibitors. See p. 337, col. 1. In other words, Saskia teaches that predefined ranges can be defined in order to classify the efficacy indicated for the flavonoid. It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize predefined ranges as suggested

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by Saskia to sort the physical-chemical properties of Yang so as to classify the compounds being screened as having good, moderate or poor anticipated efficacies in order to identify the compounds meriting further scrutiny.

- 5. With respect to the use of an oxidation potential wave, see Yang, p. 599, col. 2.
- 6. With respect to the use of the onset of oxidation, fig. 3 of Yang shows the typical voltammetric profiles for the compounds. It is noted that the various curves being shown all have similar oxidation slopes with the onset of oxidation occurring some 0.05 V prior to the  $E_{1/2}$  potential utilized by Yang. Because there is not an appreciable phenomenological distinction between when the onset of oxidation occurs and the half-wave potential occurs (i.e. the two potentials are offset by a mere voltage shift), utilizing the onset of oxidation instead of the half-wave potential would have required only routine skill in the art.
- 7. With respect to the use of a energy or transport profile, see Yang's discussion of the use of a partition coefficient on p. 600.
- 8. Claims 2 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Saskia as applied to claim 1 above, and further in view of Rapta et al (Free Radical Biology & Medicine, 18(5), 1995, pp. 901-908).
- 9. With respect to claim 2, both Yang and Saskia taught the use of swept potentials, but didn't explicitly recite the use of cyclic voltammetry to generate the voltammograms. Rapta teaches that cyclic voltammetry is a conventional manner for measuring an oxidation potential for a molecule. See fig. 1 and "Anodic oxidation" on pp. 903-905. It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of Rapta for the method of Yang and Saskia because the use of conventional potential sweep

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methods for the sweeping of Yang and Saskia requires only routine skill in the art. In addition, Rapta teaches that measuring the reduction (which would be observable in a cyclic voltammogram but not a linear voltammogram) also provides useful information about the efficacy of the monitored antioxidant (see p. 904). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize cyclic voltammetry for the measurement of Yang and Saskia so as to provide the reducing peaks and its influence on the flavonoid activity.

10. With respect to claim 7, Yang and Saskia relied only on the oxidation peak and did not teach the use of a potential for a reduction wave. However, as discussed above, Rapta teaches that the location of the reduction wave gives information about the ease of autooxidation, which impacts the antioxidant's efficacy. See p. 904. Hence, it would have been obvious to one of ordinary skill in the art at the time the invention was being made to also incorporate the potential of the reduction wave into the physical-chemical/biological relationship so as to account for the influence that autooxidation has on the flavonoid efficacy.

#### Allowable Subject Matter

- Claims 5, 6, 10-19, 26-31, 33-36, 50-53, 56, and 57 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
- 12. The following is a statement of reasons for the indication of allowable subject matter:

  With respect to claims 5 and 6, the prior art does not disclose nor render obvious all the

  cumulative limitations of claim 1 where the physical-chemical profile comprises the parameter of

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either the reversibility of one or more oxidation waves or the reversibility of one of more reduction waves. With respect to claims 10, 26, and 33, the prior art does not disclose nor render obvious all the cumulative limitations of claim 1, claims 1 and 3, or claims 1 and 4 and further comprising the use of the set forth assays of claims 10, 26, or 33 for the biological assay. Claims 11-19, 27-31, 34-36, 50-53, 56, and 57 are objected to because they depend from the above claims containing allowable subject matter.

## Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kaj Olsen whose telephone number is (571) 272-1344. The examiner can normally be reached on Monday through Friday from 8:00 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AU 1795 December 15, 2007

> KÄJ K. OLSEN PRIMARY EXAMINER

PTO/SB/08A (08-03)
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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Application Number	10/696,752	
Fitting Date	10/29/2003	•
First Named Inventor	Gilat, Sylvain	
Art Unit	unknown	
Examiner Name	unknown	
Attorney Docket Number	0126-UTL	

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Examiner Initials*	City No.	Document Number	Publication Date MM-DD-YYYY	Applicant of Clied Document	Relevant Passages or Relevant Figures Appear
		Mumber-Kind Code <sup>3 (* teres)</sup>		<del>                                     </del>	
K	A1	<sup>US-</sup> 5,874,461	02-23-1999	deChaffoy deCourcell	
VD.	A2	<sup>US-</sup> 6,121,234	09-19-2000	BENET et al.	
17)	A3	us- 6,031,076	02-29-2000	FALB et al.	
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PTO/SB/088 (08-03)

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U.S. Patent and Trademanh Office; U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number. Complete if Known flute for form 1449/PTO **Application Number** 10/696,752 **INFORMATION DISCLOSURE** Filing Date 10/29/2003 STATEMENT BY APPLICANT First Named Inventor Gilat, Sylvain Art Unit unknown (Use as many sheets as necessary) Examiner Name unknown **Attorney Docket Number** 0126-UTL of |2 Sheet 2

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initiats*	Cite No.	include name of the author (in CAPITAL LETTERS); title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
KO	C1	YANG et al. (2001) "Estimation of the antioxidant activities of flavonoids from their oxidation potentials", Analytical Sciences 17(5):599-604.	
KO	C2	BENSASSON et al. (1999) "Redox regulation of tumor cell toxicity by flavones from Lethedon tannaensis". Free Radical Biology & Medicine, 27(1/2):95-99	
KO	СЗ	MOUITHYS-MICKALAD et al. (2001) "Electrooxidation potential as a tool in the early screening for new safer Clozapine-like analogues". J. Med. Chem, 44:769-776	
KO	C4	CHENG et al. (2002) "Phenolic antioxidants: electrochemical behavior and the mechanistic elements underlying their anodic oxidation reaction". Redox Report 7(6):395-402	
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Art Unit unknown Examiner Name unknown Attorney Docket Number 0126-UTL

Exeminer Initials*	Cita No.	Document Number	Publication Date MM-DD-YYYY	Name of Patenton or Applicant of Cited Document	Pages, Columna, Lines, Where Relevant Passages or Relevant Figures Appear
VO	1	Number-Kind Code <sup>2 of Install</sup> US- 4,997,526	03- 05-1991	Robblee	
TU	2	<sup>US</sup> - 5,574,656	11-12-1996	Agrafiotis et al.	
$\dashv$	3	US- 5,684,711	11-04-1997	Agrafiotis et al.	
+-	4	US- 5,763,479	08-09-1998	Chayen et al.	
-1-	5	<sup>US-</sup> 5,901,069	05-04-1999	Agrafictis et al.	
-	6	<sup>US-</sup> 6,306,595	10- 23-2001	Hendry	
+	7	US- 6,344,330	02-05-2002	Eliman et al.	
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	12	US- 2002/0034537	03-21-2002	Schulze et al.	
_	13	US- 2002/0123069	09-05-2002	Johnson	
1	14	US- 2003/0014191	01-16-2003	Agrafiotis et al.	
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